

IN THE CLAIMS:

1-4. (Canceled)

5. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein amino acids located in at least two beta strands of at least two beta sheets of the protein are mutagenized.

6. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein amino acids located in three beta strands of two antiparallel beta sheets of the protein are mutagenized.

7. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein the protein is a vertebrate gamma-crystallin.

8. (Canceled)

9. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein the protein is a gamma-II-crystallin.

10. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein an amino acid located within the protein is mutagenized in a region of the beta sheet that is accessible to a solvent.

11. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein an amino acid is mutagenized in a region of the protein selected from the group consisting of a  $\beta$ -sheet structure of a domain of the protein and a  $\beta$ -sheet structure of a subunit of the protein.

12-13. (Canceled)

14. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein the new antigen binding specificity is for a compound selected from the group consisting of estradiol and BSA- $\beta$ -estradiol-17-hemisuccinate.
15. (Canceled)
16. (Previously presented) A composition comprising the mutagenized gamma-crystallin polypeptide of claim 42 and at least one other protein or non-protein substance.
- 17-25. (Canceled)
26. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 7, wherein the vertebrate is selected from the group consisting of a bovine, a rodent, a bird, and a fish.
27. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein an amino acid of the protein is mutagenized in a region of the beta sheet that is accessible to a binding partner.
28. (Previously presented) The mutagenized gamma-crystallin polypeptide of claim 42, wherein an amino acid is mutagenized in a  $\beta$ -sheet structure of a subunit of the protein.
- 29-41. (Canceled)
42. (Currently amended) A mutagenized gamma-crystallin polypeptide with a new binding activity towards a binding partner, wherein amino acids on a surface of the gamma-crystallin polypeptide are mutagenized, and further wherein:
  - the amino acids that are mutagenized are located in two, three, or for beta-strands of at least one beta-sheet of said gamma-crystallin polypeptide;

- said beta-sheet, said beta-strands, and said amino acids are located on a surface of said gamma-crystallin polypeptide and are thus accessible to a solvent or a binding partner; and
- the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the mutagenized gamma-crystallin polypeptide has a new binding activity towards a binding partner, with the proviso that the gamma-crystallin polypeptide without substitution, deletion, insertion, or combinations thereof has no binding activity at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution, deletion, insertion, or combinations thereof at the surface of the beta-sheet structure, the gamma-crystallin polypeptide has a new binding activity towards a binding partner.

43-46. (Canceled)

47. (Currently amended) A mutagenized gamma-crystallin polypeptide with beta-sheet structure and a new binding activity towards a binding partner, wherein amino acids on a surface of gamma-crystallin polypeptide are mutagenized, and further wherein:

- the amino acids that are mutagenized are located in two, three, or for beta-strands of at least one beta-sheet of said gamma-crystallin polypeptide;
- said beta-sheet, said beta-strands, and said amino acids are located on a surface of said gamma-crystallin polypeptide and are thus accessible to a solvent or a binding partner; and
- the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the mutagenized gamma-crystallin polypeptide has a new binding activity towards a binding partner, with the proviso that the gamma-crystallin polypeptide without substitution, deletion, insertion, or combinations thereof has no binding activity at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution, deletion, insertion, or combinations

- thereof at the surface of the beta-sheet structure, the gamma-crystallin polypeptide has a new binding activity towards a binding partner; and
- said mutagenized gamma-crystallin polypeptide is prepared by a method comprising:
    - (a) selecting a gamma-crystallin polypeptide;
    - (b) selecting a binding partner of the gamma-crystallin polypeptide;
    - (c) mutagenizing a nucleic acid molecule encoding amino acids on a surface of the gamma-crystallin polypeptide, wherein:
      - (i) said amino acids to be mutagenized being are located in two, three, or four beta-strands of at least one beta-sheet of said gamma-crystallin polypeptide;
      - (ii) said beta-sheet, said beta-strands, and said amino acids are located on a surface of said gamma-crystallin polypeptide and are thus accessible to a solvent or a binding partner; and
      - (iii) the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof;
    - (d) expressing the mutagenized nucleic acid molecule of step (c) in order to produce the mutagenized gamma-crystallin polypeptide;
    - (e) contacting the mutagenized gamma-crystallin polypeptide with said binding partner of step (b); and
    - (f) selecting and isolating a mutagenized gamma-crystallin polypeptide with a new binding activity towards the binding partner of step (b).

Please add the following new claims:

48. (New) A mutagenized bovine gamma-II-crystallin polypeptide with a new binding activity towards a binding partner, wherein amino acids on a surface of a bovine gamma-II-crystallin of SEQ ID NO: 22 is mutagenized, and further wherein:

- the amino acids that are mutagenized are selected from the group consisting of Lys 3, Thr 5, Tyr 7, Cys 16, Glu 18, Ser 20, Arg 37, and Asp 39 of the bovine gamma-II-crystallin of SEQ ID NO: 22;
- said beta-sheet, said beta-strands, and said amino acids are located on a surface of said gamma-crystallin polypeptide and are thus accessible to a solvent or a binding partner; and
- the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the mutagenized gamma-crystallin polypeptide has a new binding activity towards a binding partner, with the proviso that the gamma-crystallin polypeptide without substitution, deletion, insertion, or combinations thereof has no binding activity at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution, deletion, insertion, or combinations thereof at the surface of the beta-sheet structure, the gamma-crystallin polypeptide has a new binding activity towards a binding partner.

49. (New) The mutagenized bovine gamma-II-crystallin of claim 48, wherein the mutagenized bovine gamma-II-crystallin has a new antigen binding specificity for a compound selected from the group consisting of estradiol and BSA- $\beta$ -estradiol-17-hemisuccinate, and further wherein the protein has an amino acid sequence comprising one of SEQ ID NO: 19 and SEQ ID NO: 21.
50. (New) The mutagenized gamma-crystallin polypeptide of claim 42, wherein the mutagenized gamma-crystallin polypeptide is a mutagenized gamma-II-crystallin polypeptide, and further wherein the mutagenized gamma-II-crystallin polypeptide comprises at least one amino acid substitution in each of three beta-strands of the N-terminal beta-sheet relative to the wild-type gamma-crystallin polypeptide upon which the mutagenized gamma-crystallin polypeptide is based.
51. (New) The mutagenized gamma-crystallin polypeptide of claim 50, wherein each amino acid substitution occurs at an amino acid selected from the group

consisting of Lys 3, Thr 5, Tyr 7, Cys 16, Glu 18, Ser 20, Arg 37, and Asp 39 of the bovine gamma-II-crystallin of SEQ ID NO: 22.

52. (New) The mutagenized gamma-crystallin polypeptide of claim 51, wherein the mutagenized gamma-crystallin polypeptide is present in a library of mutagenized gamma-crystallin polypeptides, and further wherein different members of the library comprise different amino acid substitutions at one or more amino acids selected from the group consisting of Lys 3, Thr 5, Tyr 7, Cys 16, Glu 18, Ser 20, Arg 37, and Asp 39 of the bovine gamma-II-crystallin of SEQ ID NO: 22.
53. (New) The mutagenized gamma-crystallin polypeptide of claim 52, wherein the library is a phage display library and the mutagenized gamma-crystallin polypeptide is displayed on by the phage.
54. (New) A mutagenized gamma-crystallin polypeptide with a new binding activity towards a binding partner, wherein amino acids on a surface of the N-terminal beta-sheet of the gamma-crystallin polypeptide are mutagenized, and further wherein:
  - the amino acids that are mutagenized are located in two, three, or for beta-strands of the N-terminal beta-sheet of said gamma-crystallin polypeptide;
  - said beta-sheet, said beta-strands, and said amino acids are located on a surface of said gamma-crystallin polypeptide and are thus accessible to a solvent or a binding partner; and
  - the mutagenizing comprises amino acid substitutions, such that the mutagenized gamma-crystallin polypeptide has a new binding activity towards a binding partner, with the proviso that the gamma-crystallin polypeptide without substitution has no binding activity at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution at the surface of the beta-sheet structure, the gamma-crystallin polypeptide has a new binding activity towards a binding partner.

55. (New) The mutagenized gamma-crystallin polypeptide of claim 54, wherein the mutagenized gamma-crystallin polypeptide is a mutagenized gamma-II-crystallin polypeptide.
56. (New) A mutagenized gamma-crystallin polypeptide with beta-sheet structure and a new binding activity towards a binding partner, wherein amino acids on a surface of the N-terminal beta-sheet of the gamma-crystallin polypeptide are mutagenized, and further wherein:
- the amino acids that are mutagenized are located in two, three, or for beta-strands of the N-terminal beta-sheet of said gamma-crystallin polypeptide;
  - said beta-sheet, said beta-strands, and said amino acids are located on a surface of said gamma-crystallin polypeptide and are thus accessible to a solvent or a binding partner; and
  - the mutagenizing comprises amino acid substitutions, such that the mutagenized gamma-crystallin polypeptide has a new binding activity towards a binding partner, with the proviso that the gamma-crystallin polypeptide without substitution has no binding activity at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution at the surface of the beta-sheet structure, the gamma-crystallin polypeptide has a new binding activity towards a binding partner; and
  - said mutagenized gamma-crystallin polypeptide is prepared by a method comprising:
    - (a) selecting a gamma-crystallin polypeptide;
    - (b) selecting a binding partner of the gamma-crystallin polypeptide;
    - (c) mutagenizing a nucleic acid molecule encoding amino acids on a surface of the N-terminal beta-sheet of the gamma-crystallin polypeptide, wherein:
      - (i) said amino acids to be mutagenized are located in two, three, or four beta-strands of the N-terminal beta-sheet of said gamma-crystallin polypeptide; and

- (ii) said beta-sheet, said beta-strands, and said amino acids are located on a surface of said gamma-crystallin polypeptide and are thus accessible to a solvent or a binding partner; and
  - (d) expressing the mutagenized nucleic acid molecule of step (c) in order to produce the mutagenized gamma-crystallin polypeptide;
  - (e) contacting the mutagenized gamma-crystallin polypeptide with said binding partner of step (b); and
  - (f) selecting and isolating a mutagenized gamma-crystallin polypeptide with a new binding activity towards the binding partner of step (b).
57. (New) The mutagenized gamma-crystallin polypeptide of claim 56, wherein the mutagenized gamma-crystallin polypeptide is a mutagenized gamma-II-crystallin polypeptide.